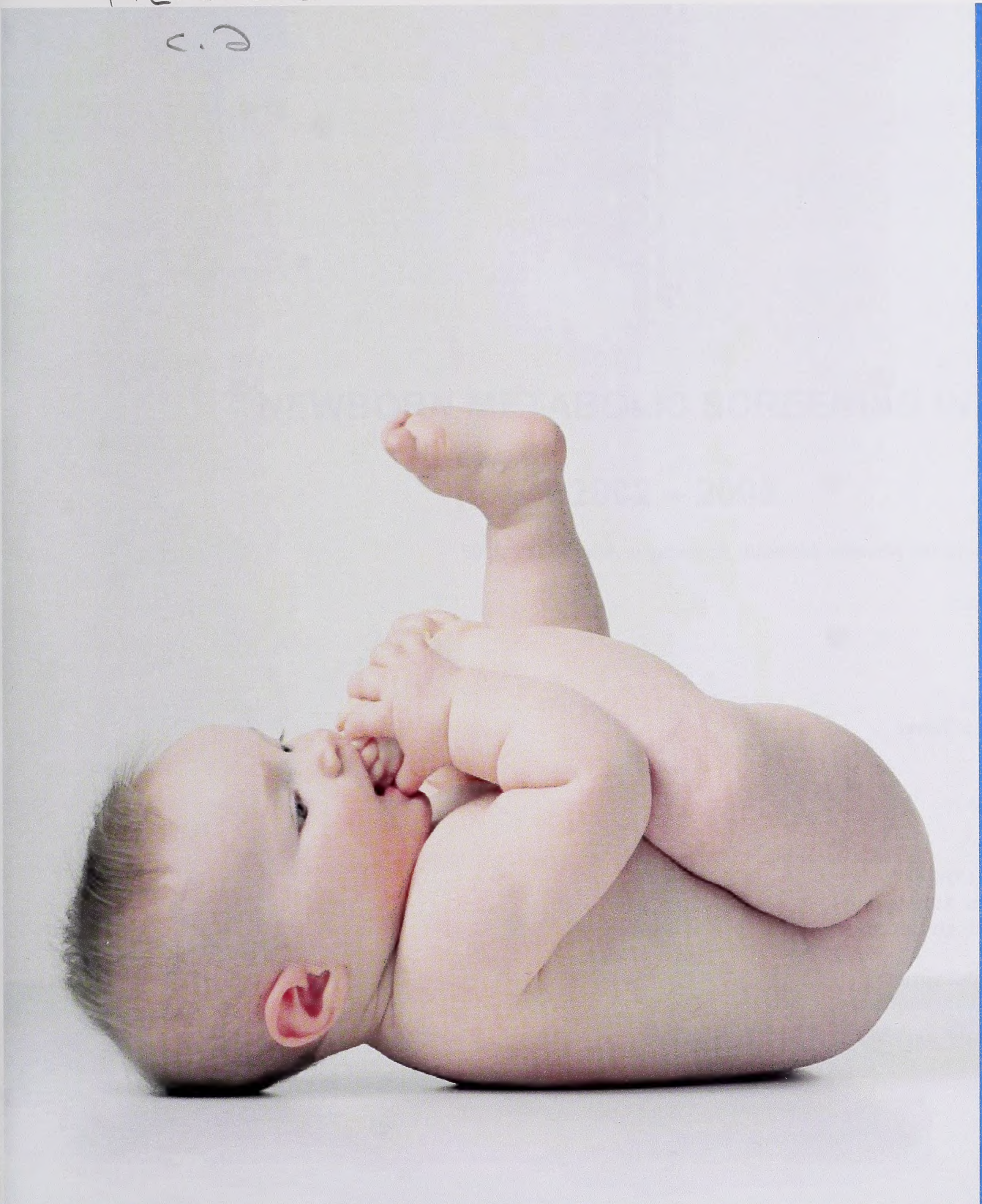
AL.2.2007-58
c.2



REPORT

Newborn Metabolic Screening in Alberta
2002-2005

Alberta Health and Wellness

November 2006

Alberta Health and Wellness (2006) *Newborn Metabolic Screening in Alberta 2002-2005*

For more information contact:

Provincial Health Office
Public Health Division
Alberta Health and Wellness
24th Floor Telus Plaza North Tower
10025 Jasper Avenue
PO Box 1360 STN MAIN
Edmonton, Alberta T5J 2N3
CANADA

Telephone: 1-780-427-4518
Toll Free: 310-0000 (in Alberta only)
Website: www.health.gov.ab.ca

ISBN: 0-7785-3500-2 (print)
ISBN: 0-7785-3501-0 (internet)

NEWBORN METABOLIC SCREENING IN ALBERTA

2002 – 2005

Public Health Division
Alberta Health and Wellness

November 2006

Digitized by the Internet Archive
in 2016

https://archive.org/details/newbornmetabolic00albe_0

TABLE OF CONTENTS

1. Executive Summary 4

2. Introduction 5

3. Background 6

4. The Alberta Newborn Metabolic Screening Program 8

5. Program Results: January 2002 to December 2005 12

6. Conclusions 26

EXECUTIVE SUMMARY

This report provides an overview of the Newborn Metabolic Screening (NMS) Program in Alberta from 2002 to 2005. A brief history and an overview of the roles of stakeholders in the current operation of the program are provided. The program standards and guidelines are used as a framework for review and reporting on the program. Data from the NMS application are used to report on key program indicators. During this period, the Alberta NMS program screened for three conditions: phenylketonuria, congenital hypothyroidism and biotinidase deficiency.

Results from this analysis indicate that the program is functioning effectively. Greater than 99 per cent of infants born in Alberta receive an initial screen. More than 98 per cent of infants have the initial screen collected in the target period (between 24 hours and seven days after birth). Approximately one out of every 2,200 infants (74 in total) have screened positive for one of the three conditions since January 1, 2002.

The review of the program data for four years provided an opportunity to examine the data process in detail.

INTRODUCTION

Each year, a small number of Alberta babies are born with metabolic diseases that can lead to severe developmental disabilities, developmental delay and other health problems. These diseases can be detected through a simple blood test performed between 24 hours and seven days following birth. If a metabolic disease is detected, it can be treated successfully and adverse outcomes avoided. The test is available to all babies born in Alberta.

Metabolic disorders are rare but can have devastating and irreversible outcomes if not diagnosed early and treated promptly. The goal of the newborn metabolic screening program is early recognition and treatment of these disorders, before the onset of symptoms.

This report provides an overview of the Alberta Newborn Metabolic Screening (NMS) program. It examines approximately 160,000 infants born in Alberta between January 1, 2002 and December 31, 2005. The objectives of this report are:

- To describe the accomplishments of Alberta Newborn Metabolic Screening Program in meeting the program standards and guidelines, using data gathered in the NMS application.
- To engage internal stakeholders in program dialogue to further improve the program.
- To create a baseline for future program evaluation.

BACKGROUND

Newborn Metabolic Screening

Currently, three metabolic disorders are tested for in Alberta – phenylketonuria, congenital hypothyroidism and biotinidase deficiency.

Phenylketonuria (PKU) is an inherited disorder of phenylalanine metabolism, which, if untreated, causes severe developmental problems. The condition cannot be detected on clinical grounds in the newborn period. Initiation of a diet low in phenylalanine by three weeks of age prevents the occurrence of brain damage.

The incidence in Alberta is approximately one in 14,000 births with two to four new cases detected each year.

Congenital Hypothyroidism (CH) is a disorder in which thyroid function is abnormal and requires immediate and life long treatment. Most babies appear healthy in the newborn period but may have prolonged neonatal jaundice. Clinical features associated with CH such as constipation, hoarse cry and slow feeding may be missed early in life and cannot be relied upon for diagnosis. Developmental delay may occur if the condition is not treated promptly with thyroxine.

The incidence in Alberta is approximately one in 3,500 births with 10 to 15 cases detected each year.

Biotinidase Deficiency. Biotin is a co-factor for a number of enzymes in metabolic pathways. In biotinidase deficiency, biotin cannot be recycled for further use by the body and biotin deficiency develops. This inherited condition can present in a number of different ways. Some infants have seizures and developmental delay with deafness and visual problems. Others have hair loss and eczema. Some individuals are asymptomatic. Treatment with biotin, one of the B group of vitamins, is simple and effective.

The incidence is approximately one in 80,000 births, with one new case of biotinidase deficiency detected every two years in Alberta.

Babies identified with one of these metabolic disorders are referred by the NMS program to a specialist for diagnosis, clinical assessment and management. Management of all three conditions, through special diets and supplements, is life-long. PKU is managed with a lifelong diet low in phenylalanine. In congenital hypothyroidism, thyroid hormone replacement provides effective treatment. Biotinidase deficiency is easily managed with biotin, one of the "B" group vitamins. The special diets and treatment (except for transportation for visits to the metabolic clinic) are provided to Alberta families free of charge through the metabolic clinics located in Edmonton and Calgary.

Population screening of all newborns for metabolic disorders also reduces the financial burden associated with long-term care for affected individuals. While these conditions are relatively rare, if they are left untreated, the cost to the individual and to the health care services delivery system can be substantial. For every case of PKU detected through early screening, it has been estimated that about $293,000 in long-term care costs are avoided.[1] Overall in Alberta, the early detection of metabolic disorders through the NMS screening program helps reduce the long-term care costs of affected children by an estimated $700,000 per year.

---

[1] Premier's Award of Excellence Submission (2004) Newborn Metabolic Screening PAE Submission, Project Team.

THE ALBERTA NEWBORN METABOLIC SCREENING PROGRAM

The Alberta Newborn Metabolic Screening Program started in 1967 with the introduction of screening for phenylketonuria. Screening for congenital hypothyroidism was added in 1977, and screening for biotinidase deficiency was added in 1990. These three conditions were identified in the *Alberta Public Health Act* on October 15, 2000 as diseases under surveillance.

Earlier discharge of healthy infants from birthing facilities in the late 1990s led to a concern that the timely screening of all Alberta infants for metabolic disorders would be more difficult to achieve. As the blood samples for the screens are best collected after 24 hours of age, when many infants have left the hospital, the responsibility for obtaining the screen fell largely to public health nurses on community visits and to midwives.

Newborn Metabolic Screening (NMS) Standards and Guidelines

A multidisciplinary advisory committee was convened in 1997 to develop standards and guidelines for the Newborn Metabolic Screening Program. The standards dealt with the process, timeliness and pathways of communication between the stakeholders and set in place specific benchmarks for program activities.

The goals of the Alberta Newborn Metabolic Screening Program are:

1) 100 per cent of infants born in Alberta will, if there is parental consent, have a metabolic screen performed on a blood sample collected between 24 hours and seven days of age, unless there is death before the sample collection.

2) 100 per cent of infants requiring repeat screening will have a repeat sample obtained within three working days of notification unless otherwise indicated by the NMS Laboratory.

3) 100 per cent of samples collected will be submitted on the requisition supplied by the Metabolic Screening Laboratory and all required information will be completely and accurately filled in.

4) 100 per cent of screens submitted to the Metabolic Screening Laboratory will be analyzed within two working days of receipt of specimen.

5) The Metabolic Screening Laboratory will report 100 per cent of clearly abnormal results to the attending physician, registered midwife and the Medical Officer of Health (MOH) of birth region within one working day.

6) 100 per cent of children with an abnormal test result will receive a timely and appropriate medical referral for follow-up and treatment.

NMS Application

To help ensure every newborn received metabolic screening within the recommended timeframe, **Alberta we//net** developed a secure web-based NMS tracking system. The system helps regional health authorities and the provincial metabolic screening laboratory track all registered births and newborn metabolic screens, and follow those babies requiring further testing.

From December 1998 to March 1999, the NMS application was piloted in three health regions. The subsequent evaluation of the pilot showed that 99.9 per cent of live births successfully received an initial screen in the pilot regions as compared to 97.9 per cent of births in the other regions. The NMS application was implemented in all the health regions in the province from October 1999 to May 2000.

How the NMS Program in Alberta Works

When a child is born in an Alberta hospital, hospital staff can access an online registry, the person directory, maintained by Alberta Health and Wellness, where they register the infant and obtain their assigned unique lifetime identifier (ULI). If the infant is eligible for health insurance in Alberta, this number will become their personal health number. The ULI is recorded by the hospital staff on the newborn metabolic screening requisition form to assist in tracking each infant. Midwives can also register home births with the local hospital and obtain ULIs for those infants.

Screening samples are collected either at the hospital, at a home birth by a midwife, or by public health nurses during a well baby visit. Due to a trend to early discharge of healthy newborns, the collection of the blood sample for the NMS is often the work of public health nurses during home visits. The process may differ slightly from health region to health region, but is consistent with overall standards and guidelines for the program.

Parents are informed of the screening program and their verbal consent to the procedure is requested. A blood drop from a heel poke sample is captured on filter paper located on the newborn metabolic screening requisition form when the infant is between 24 hours and seven days of age. The samples are sealed and transported to the Newborn Metabolic Screening Laboratory in Edmonton for metabolic analysis. The laboratory, located at the University of Alberta Hospital in Edmonton, is responsible for processing all newborn metabolic screens in Alberta.

The timing of the collection and testing of samples is important. Best practice standards indicate that the sample should be taken after the first 24 hours of life, after the first feeding so that the metabolic processes are initiated, to ensure the accuracy of the PKU testing. The sample should also be taken before the child is a week old to ensure that the sample is processed within the recommended timeframe and that appropriate action is taken before any adverse consequences to infants affected by metabolic disorders have occurred.

The process of matching the ULI, as registered with Alberta Health and Wellness and as recorded on the metabolic screen requisition, is done through the NMS application before the newborn is 11 days old. The 10-day period allows for a maximum screening age of seven days and a maximum transit time of three days, according to the standards and guidelines for the NMS program. The NMS application raises an alert when the matching has not happened after 10 full days. The matching of the screen and NMS application based on the ULI number is a key part of the newborn metabolic screening process.

The application generates an alert to the NMS co-ordinator in the health region where the baby was born to indicate a baby has not been screened. The NMS co-ordinator is responsible for ensuring that the screen is obtained as quickly as possible. When a screen is received, but no matching ULI is found, a missing birth event alert is generated by the NMS application. In this case the sample is tested and attempts are made to find the matching registered birth through the application.

The NMS application also sends an alert when collection of a repeat sample is required. There are several reasons why an alert for a repeat blood sample might be generated. In the first instance, insufficient quantity of blood, contaminated samples and the collection of blood before 24 hours of age are unsatisfactory for testing and a repeat screen is ordered. These are considered ***minor alerts*** within the NMS system. These unsatisfactory samples are tested, but results are only registered if a major abnormality is detected. Other minor alerts include results that indicate slightly elevated or borderline results, or when there is missing or erroneous demographic information.

A ***major alert*** is generated when the initial screen shows a result suggestive of one of the three metabolic disorders tested for in Alberta. The laboratory contacts the infant's physician and the nearest metabolic clinic. The family physician contacts the family, arranges for diagnostic testing and provides follow up, referrals and support to the infant and family.

Minor alerts are closed automatically upon receipt of a repeat sample or can be closed manually by the regional health authority or by the laboratory with the date of the receipt of the repeat screen or documentation of the reason the screen was not obtained (e.g. infant death, parental refusal, inability to locate infant, etc.). Major alerts are closed by the laboratory after contact with the family physician is made.

The newborn metabolic screening co-ordinator in each health region is responsible for checking the NMS application on a regular basis and ensuring follow up on the minor and major alerts, locating missing screens, and submitting repeat samples when required.

PROGRAM RESULTS: JANUARY 2002 TO DECEMBER 2005

Methods

The data for the following tables were extracted from the Newborn Metabolic Screening Application. All data were amalgamated at the provincial level by calendar year.

Limitations

There were several limitations on the data used for the following tables:

- The 2001 NMS data covers the time period from May 1, 2001 to December 31, 2001 due to the timing of the implementation of the application. The 2001 data is thus incomplete and this status report begins from January 1, 2002.

- As a preliminary step in compiling this document, the reports available to regional health authorities (RHAs) within the application were reviewed as potential sources of data. This review showed that the reports did not generate all information required. Data for this report was generated directly from the application.

- Changes made to regional health authority boundaries in 2002 have implications for the data available on a regional level. It is not currently possible to provide annual regional level data from the beginning of the program from within the NMS application.

- The NMS laboratory in Edmonton carries out all of the testing of screens from the western part of the North West Territories (NWT), but the application does not allow follow up of NWT infants electronically. There is a possibility that infants from the NWT are included in the numbers of screens received, which could then lead to more screens being reported than infants registered in Alberta.

- The NMS application receives updates from Alberta Health and Wellness for 28 days following the initial registration of the infant's ULI. Any updates or changes related to data that occur after this period are not reflected in the NMS database.

- Given current data structures and program design, it is possible only to evaluate the first program goal using the NMS application data. This limits greater evaluation of the entire function of the program.

Babies born in Alberta from January 1, 2002 to December 31, 2005

According to the NMS database, 161,176 infants were registered with Alberta Health and Wellness as newborns in Alberta during this time period.

Table One: Number of Live Births * in Alberta as recorded by NMS application

	2002	2003	2004	2005	Total 2002-2005
Number of Newborns Registered in Alberta in the NMS application[2]	38,606	40,150	40,551	41,869	**161,176**

* Excludes neonatal deaths

Discussion

The identification of a total number of births is important when assessing the success of the Alberta Newborn Metabolic Screening Program. As a population-based screening program, it aims for 100 per cent coverage. For the Alberta NMS program, this means that 100 per cent of babies who have parental consent will be screened for metabolic disorders.

The number of births registered through Vital Statistics differs from the number of newborns registered in the person directory and the number of newborns in the NMS application. The differences between these are explained below.

Table Two: Number of births/newborns in Alberta

	2002	2003	2004	2005
Number of Live Births in Alberta	n	n	n	n
Vital Statistics	38,749	40,341	40,742	42,011
Alberta Person Directory	38,854	40,447	40,867	42,145
NMS application	38,606	40,150	40,551	41,869

Discussion

Alberta Vital Statistics maintains the legal registry for all live births, stillbirths, death and marriages within the provincial jurisdiction. The main form for registering a live birth is completed by the parents, while physicians or other birth attendants are also required to report the birth on a notice of birth form.

---

[2] Source: NMS database.

The **Alberta Person Directory** is the registry of Alberta Health and Wellness. ***Newborns*** and ***stakeholders*** are identified within the registration system, and the newborn information is used to populate the NMS database. Screens and newborn registrations are matched within the NMS application.

The **NMS application** reconciles screen requisition forms from the regions and birth registrations from the person directory in order to identify number of infants screened.

There are a number of reasons why each of these registries may differ slightly in the number of newborns recorded. A few illustrative examples follow:

The databases may differ in what they record as ***newborns*** in their registries. For example, if a child is born to Alberta parents outside of the province, the child, when registered upon return to Alberta may not be registered as a ***newborn*** in the person directory. In that situation, the child's first contact with the Alberta medical system may be when the parents register their child for a health card upon return to the province. The child may be registered as a ***stakeholder*** rather than a ***newborn***. If such a child has not been screened immediately after being born out of province, that child may be missed in the NMS application as only those infants recorded as ***newborns*** will be included in the NMS application.

Newborns who are dependents of federally sponsored groups (those who fall under First Nations and Inuit Health Branch, penitentiary, military or RCMP jurisdiction) may have been dealt with inconsistently within the NMS system.

There may be duplicates present in the systems. For example, if the parents have different last names, the newborn may first be registered under the last name of the mother for a ULI and then later be officially registered with the father's last name. The child then has two ULIs in the person directory maintained by Alberta Health and Wellness. An alert would be generated within the NMS application when it appeared as if the infant had not been screened as the screening requisition would only match one of the ULIs. The laboratory and regional staff work together to identify a child with multiple ULIs and one of the birth events is cancelled manually by the laboratory.

The regional health authorities may have different ways of dealing with stillbirths and neo-natal deaths. In some regional health authorities, a stillborn child or a neo-natal death would be registered in the person directory, but other regions might not process the situation the same way. Much depends on the circumstances and context of the death and the fragility of the infant at birth. Each regional health authority and the attending physician may have different ways to reflect stillborn or neonatal deaths in NMS. Stillborn babies are infrequently registered in the person directory, while Vital Statistics has very clear guidelines as to the registration of the stillborn infants in a separate registry.[3] About 120 to 180 neo-natal deaths (generally defined as the death of a live-born infant in the first 28 days of life[4]) are registered in the person directory each year which is appropriate given the current standards and guidelines for the program.

As a population-based screening program, it is essential that no child is missed in the process. For this reason, stillborns, neo-natal deaths, and out of province residents may be included in the totals of the NMS database.

For this report, the NMS data were examined closely, and stillborns, neo-natal deaths and one of the records for those infants screened under multiple ULIs were removed from the total number of newborns registered, giving the results recorded in Table One. This elimination provides for greater accuracy when assessing the number of newborns eligible for inclusion into the NMS screening program each year. The number of newborns recorded in the NMS database will be used as the denominator for this status report. Reconciliation of regional, provincial and national databases that record births should be addressed in the future to facilitate accurate and thorough NMS program evaluation.

The reconciliation of these major databases may be an important issue in determining the coverage of the program and ensuring that no child is missed in the NMS program. With a stated goal of screening 100 per cent of all newborns whose parents consent to the screening process, agreement on exact numbers of children being born in the province is critical in order to monitor program progress and inclusion. Further agreement is needed on the source of the data, or the reconciliation of the data for the total number of infants born in Alberta in order to most accurately measure program goals.

---

[3] Births 2003 (July 2005) Statistics Canada, Health Statistics Division. Available on-line at: http://www.statcan.ca/cgi-bin/downpub/listpub.cgi?catno=84F0210XIE2003000

[4] WHO website. Neo-natal death. Available on-line at: http://www.who.int/reproductive-health/publications/MSM_98_1/MSM_98_1_glossary.en.html

Newborns receiving an initial screen

Table Three: Number of newborns receiving an initial screen by year

NMS	2002		2003		2004		2005	
	n	%	n	%	n	%	n	%
Newborns receiving initial screen	38,462	99.6	40,005	99.6	40,462	99.8	41,774	99.8
Not screened (reason provided)	144	0.4	145	0.4	89	0.2	125	0.2
Not screened (reason NOT provided)	0	0	0	0	0	0	0	0
Total newborns in NMS application	**38,606**	**100**	**40,150**	**100**	**40,551**	**100**	**41,869**	**100**

Discussion

According to the NMS application, in 2005 greater than 99.8 per cent of all newborns in Alberta received an initial screen. The reasons for the less than one per cent of children not being screened are reported below. According to the NMS application, no birth registered in the NMS application has been missed by the screening program since the application began tracking of newborns province wide in May 2001.

Reasons for infants NOT receiving an initial screen

Table Four: Reasons for not receiving initial screen by year

NMS	2002 n	2003 n	2004 n	2005 n
Not screened (reason provided)	144	145	89	125
Reasons				
• Other	98	83	40	75
• Out of province[5]	37	43	28	16
• Parental refusal	6	15	17	27
• Physician refusal	1	1	1	0
• Unable to locate the family after released from hospital	2	3	3	7
Total not screened	**144**	**145**	**89**	**125**

Discussion

Each year, a small number of infants born in Alberta are not screened (Table Four) and a reason for that decision is recorded. In order to ensure that no infant is missed in the screening process, it is important to understand the implications of the reasons given in Table Four and make appropriate adjustments in the application or program to reach the stated goals.

---

[5] Out of province refers to those babies who, for whatever reason, relocate to another province shortly after birth.

Currently less than one per cent of infants born in Alberta are not screened through the newborn metabolic screening process. The goal of the program is to provide screening for 100 per cent of those infants whose parents consent to the procedure. In Alberta, parental refusals have accounted for a total of 65 infants not being screened through the program since January 1, 2002, through to the end of December 2005. Parental refusals account for less than 0.05 per cent of the total number of infants born.

Other reasons for not receiving a screen are listed below.

- Babies whose parents are from out of province may be born and registered in Alberta, but newborn screening follow up may be done when they return to their home province. In this case, information will not be available in the NMS application about the child, but the laboratory or public health unit will follow up with the home province to ensure screening is done. Babies born to Alberta parents living out of province will not be registered in the NMS system unless the parents make an application to have the child registered as a newborn with Alberta Health and Wellness.

- Physicians can also refuse a screen on behalf of an infant, and this is most often done in circumstances where the newborn is extremely ill and in palliative care.

- Sometimes the regional health authorities are unable to locate the family once the mother and newborn have been released from hospital. If the hospital is concerned that it may be difficult to follow up with the family in the community, testing may be carried out at the hospital, even though this is less than optimal timing for the screens (such as less than 24 hours of age). Babies who are adopted through closed adoptions may occasionally be difficult to locate once they leave the hospital. The public health unit will contact the adoption agency to ensure follow up.

- Newborns have also occasionally been screened under a ULI other than the one they were initially given in the hospital. Sometimes confusion over last name (mother's, father's or baby's) may result in the generation of an additional ULI. Attempts are made to reconcile the ULIs during the NMS screening process and determine if the child has actually been screened.

- The documented process in the case of neo-natal death or stillborn is to register the infant with a ULI and to indicate status on the NMS requisition and to submit it, without a sample, to the laboratory. This process prevents the generation of an alert and the attempted follow up by the NMS regional health authority contact. However, it is not officially required to register the stillborns or neo-natal death and the regional health authorities follow different processes around these events.

The category of ***other*** reasons for not being screened needs to be better identified as it accounts for approximately 50 per cent of the reasons for not being screened. It may be that some of those in the ***other*** category belong in another category and have been inappropriately coded to the category of **"other."** It may also be that these numbers reflect reasons not contemplated when the NMS application was first created. Further investigation of the ***other*** category will provide more information to identify possible disconnects in the screening process.

The reasons for infants not receiving a screen must be closely monitored to ensure that as many children as possible have the opportunity to be screened through the program. Of key importance is the category where regional staff are unable to locate the families once they are released from hospital. These infants do not receive screens and are at risk for developing negative outcomes of metabolic disease. Co-ordination of screening efforts between provinces, a public health campaign to potential parents regarding the importance of metabolic screening and ensuring tracking of infants once they leave from the hospital are all potential areas of focus to improve the program.

Quality of samples submitted for testing

Table Five: Adequacy of sample submitted, by year

Note: This table includes all samples submitted (initial and all subsequent repeat samples)

NMS	2002		2003		2004		2005	
	n	%	n	%	n	%	n	%
Number of adequate samples	40,001	98.7	41,517	98.4	41,997	98.8	43,445	99.4
Number of inadequate samples	543	1.3	662	1.6	496	1.2	266	0.6
Total samples	**40,598**	**100**	**42,227**	**100**	**42,542**	**100**	**43,711**	**100**
Reasons for inadequacy								
• Not sufficient quantity (NSQ)	297		316		139		66	
• Unsuitable	99		148		175		60	
• Taken < 24 hours after birth	147		198		182		140	
Total repeat screens required due to inadequate sample	**543**		**662**		**496**		**266**	

Discussion

When and how a sample is taken will influence the quality of the screen received by the laboratory. The guidelines state that the sample should be collected on the appropriate material (filter paper requisitions) and that the sample should be collected after the infant is 24 hours old and before seven days have passed.

Each screening requisition contains four designated areas for application of the blood sample. A blood spot punch is taken from one of these areas by the NMS laboratory staff for testing. Any inadequate sample will generate an alert within the system, resulting in a request to the health region contact for a repeat collection. Not sufficient quantity (NSQ) samples do not provide enough blood to run all the tests, while those tests taken before 24 hours after birth has elapsed will not provide reliable results, especially for PKU. ***Unsuitable*** samples may include those that have too much tissue fluid, appear to be contaminated, have blood that is severely clotted or layered, or are on damaged filter paper. The laboratory staff attempts to locate an appropriate sample on the filter paper and will run the test, regardless of the quality of the initial sample. This is done as it may not be possible to obtain an additional sample. A repeat sample is requested from the RHA to confirm the result if a poor quality sample is received.

Inadequate samples make up about one per cent of all samples taken in Alberta. A training video and manual describing appropriate sample collection technique is available to all RHAs in order to facilitate correct sample collection techniques.

The numbers of inadequate samples dropped between 2004 and 2005. Possible reasons for improvement in quality may reflect more experience with the screening process, increased communication between the laboratory and health regions, or the training sessions in sample collection given in various health regions.

Maintaining a high quality of sample collection for the NMS screen, together with complete and accurate demographic information, is essential for the success of the program. High quality screens ensure that the test is of maximum accuracy and the infant has the best chance of being identified through the screening program. It also reduces the need for repeat screens, which saves time and resources. Ongoing educational opportunities and training of staff in the field are important to maintain high standards of screening.

Requests for repeat screens completed

Table Six: Required repeat screens due to inadequacy of initial sample, by reason and by year

Not sufficient quantity	2002	2003	2004	2005
	n	n	n	n
Repeats required	297	316	139	66
Repeats completed	293	304	136	60
Repeats not completed	4	12	3	6
Percentage repeats completed	**98.7**	**96.2**	**97.8**	**90.9**

Unsuitable sample	2002	2003	2004	2005
	n	n	n	n
Repeats required	99	148	175	60
Repeats completed	92	141	170	59
Repeats not completed	7	7	5	1
Percentage repeats completed	**92.9**	**95.3**	**97.1**	**98.3**

Sample taken < 24 hours after birth or Timing of Sample not indicated	2002	2003	2004	2005
	n	n	n	n
Repeats required	147	198	182	140
Repeats completed	50	48	60	33
Repeats not completed	97	150	122	107
Percentage repeats completed	**34.0**	**24.2**	**33.0**	**23.6**

Discussion

The percentage of repeated screens completed is lower for the samples taken before 24 hours has passed after birth than for either the unsuitable or NSQ samples. Samples taken before 24 hours of age are often those taken in the hospital setting, and are not as reliable for the metabolic tests, particularly PKU, as those taken in the 24 hour to seven day optimal time period. This pattern holds true since the beginning of use of the application and may be somewhat misleading. Often these particular samples do not need to be repeated as follow up with the regional health authority contact showed that they were actually taken after 24 hours had passed. In this case the alert is closed without a repeat screen being performed as is appropriate given the circumstances. Another reason that repeat screens were not indicated to have been repeated is that testing may have been done in another laboratory that does not share data with the NMS application.

The reporting of repeat screen alerts should be reviewed in the future.

Meeting Timing Standards

Table Seven: Birth to Initial Sample Collection (within Standards and Guidelines)

	2002	2003	2004	2005
Number of Days from birth to sample collection	**n**	**n**	**n**	**n**
1	12,740	13,098	13,126	14,396
2	16,727	17,895	18,141	17,592
3	5,919	5,973	6,114	6,454
4	874	914	809	957
5	515	473	507	604
6	398	354	399	482
7	681	705	695	666
Sample collected >=1 day and <= 7 days (as per Standards and Guidelines)	**37,943 (98.4%)**	**39,548 (98.5%)**	**39,884 (98.3%)**	**41,151 (98.4%)**
Total samples	**38,466**	**40,024**	**40,470**	**41,813**

Table Eight: Birth to sample collection

	2002		2003		2004		2005	
	n	**%**	**n**	**%**	**n**	**%**	**n**	**%**
Samples collected < 24 hours	89	0.23	136	0.34	93	0.23	85	0.20
Samples collected > than 7 days	480	1.25	458	1.14	580	1.43	545	1.30
Suspected data error[6]	43	0.11	18	0.04	6	0.01	32	0.08
Total Samples collected outside of standards	**612**	**1.59**	**612**	**1.52**	**679**	**1.67**	**662**	**1.58**
Total samples[7]	**38,466**	**100**	**40,024**	**100**	**40,470**	**100**	**41,813**	**100**

Discussion

The optimal time for sample collection is between 24 hours and seven days of age. This allows for the metabolic processes to begin after the first feeding, but also ensures that screening is done early enough to make a significant difference in the health outcome of the child if metabolic disorders are detected.

---

[6] For example the screening date is listed as occurring before the birth date

[7] Note that these numbers will not reconcile with line one of Table Three. Table Seven includes multiple screens for the same infant (as is occasionally done) resulting in slightly higher numbers.

About 98 per cent of samples are being taken within the optimal time frame as laid out in the standards and guidelines. Just over one per cent of screens each year are taking longer than the maximum seven days recommended, and about 0.2 to 0.3 per cent of samples are being collected too soon, resulting in a repeat sample request. The range of days from birth to sample collection recorded in the database are from eight days to up to 155 days. This may also include data entry errors. Obvious data errors (such as recording the taking of a sample before the birth date of the infant) are less than 0.1 per cent of all data but other data errors may not be so easily identifiable and fall within the normal range of the data seen here.

The timing of various steps in the NMS program is critical to the operation and ultimate success of the program. This analysis shows that the first step of the program is generally happening in a timely manner, according the standards and guidelines of the program. Further data regarding the timing of samples, screening, testing, diagnostics and follow up management and care are important in order to assess and evaluate the NMS program.

Final results of the Newborn Metabolic Screening Program

Table Nine: Final screen alerts of each of the three conditions by year as recorded in NMS application

NMS Test	2002		2003		2004		2005	
	n	%	n	%	n	%	n	%
Amino Acids								
• Normal	38,006	98.80	39,416	98.47	40,034	98.92	41,372	98.95
• Minor	21	0.05	18	0.04	19	0.05	35	0.08
• **Major (PKU)**	**1**	**0.00**	**4**	**0.01**	**3**	**0.01**	**2**	**0.00**
• Other (not classifiable)	440	1.14	591	1.48	416	1.03	400	0.96
Total	**38,468**	**98.86**	**40,029**	**98.52**	**40,472**	**98.97**	**41,809**	**100**
Thyroid Stimulating Hormone (TSH)								
• Normal	38,374	99.76	39,929	99.75	40,360	99.72	41,664	99.65
• Minor	74	0.19	69	0.17	77	0.19	127	0.030
• **Major (Congenital Hypothyroidism)**	**14**	**0.04**	**11**	**0.03**	**24**	**0.06**	**11**	**0.03**
• Other (not classifiable)	6	0.02	20	0.05	11	0.03	7	0.02
Total	**38,468**	**99.98**	**40,029**	**99.95**	**40,472**	**99.97**	**41,809**	**100**
Biotinidase								
• Normal	38,451	99.96	39,997	99.92	40,460	99.97	41,795	99.97
• Minor	2	0.01	3	0.01	2	0.00	4	0.01
• **Major (Biotinidase Deficiency)**	**0**	**0.00**	**2**	**0.00**	**0**	**0.00**	**2**	**0.00**
• Other (not classifiable)	15	0.04	27	0.07	10	0.02	8	0.02
Total - final screens	**38,468**	**99.96**	**40,029**	**99.93**	**40,472**	**99.98**	**41,809**	**100**

N.B. The 'Other' category includes those results which were not classifiable by the result code (e.g. inadequate, <24 hrs, minor elevations of other amino acids).

Discussion

Final screening results for the program reveal that from January 1, 2002 to December 31, 2005, 74 infants (about one in every 2,200 babies) were identified with one of the three disorders currently screened for in Alberta. Congenital hypothyroidism was the most common disorder identified through newborn metabolic screening as 60 infants were identified during this time period. Ten infants screened positive for PKU and four infants screened positive for biotinidase deficiency during this 48 month period.

The *minor* category includes those infants identified as having elevated (such as amino acids, TSH) or lowered (such as biotinidase) levels during testing. Repeat tests are requested for each of the infants identified as minor alerts. The repeat tests are generally negative but infants may be identified for follow up with their family physician or a specialist, to ensure the healthy development of the child. Data from follow up testing and assessments are not available to the NMS program for further analysis of those infants who fall into this category.

The ***other*** category includes unsuitable and inadequate samples, those that are of not sufficient quantity, those taken before the infant is 24 hours old and missing registrations. The tests for amino acids are most sensitive to timing as they are most accurate after baby is 24 hours of age, hence the larger number of ***other*** results in this category.

The NMS screening results recorded in Table Nine are not diagnostic results. It is not possible to assess from the current application the correlations between the screening results and the diagnostic outcomes. Diagnostic data is available from physician billing records in most cases and a match on ULI could provide an indication of the outcome of the screening program and a method to investigate false positive and false negative rates at a future date.

LIBRARY AND ARCHIVES CANADA
Bibliothèque et Archives Canada
3 3286 53530567 2

CONCLUSIONS

Goal 1 of the NMS Program standards and guidelines states that: "100 percent of infants born in Alberta will, if there is parental consent, have a metabolic screen performed on a blood sample collected between 24 hours and seven days of age, unless there is death before the sample collection. " The data in the report shows that:

- 100 per cent of infants in the NMS application have an initial screen or a recorded refusal or other reason for not screening.
- Greater than 99 per cent of newborns in the NMS application receive an initial screen.
- Greater than 98 per cent of newborns screened have the initial sample collected in the target period.

Further evaluation of NMS program standards will require data from other sources. For example, physician billing data can provide an effective way to follow up on infants identified through the NMS screening process. The additional diagnostic information would allow program stakeholders to ascertain the accuracy of the screening program and ensure that follow up is both timely and appropriate.

Based on discussions with regional health authority and laboratory staff, the process of developing the NMS program has resulted in stronger communication between the regions and lab. The data sharing infrastructure of the application has supported the ongoing development of the program. The application is flexible and adaptable to the realities of front line work in the regions. Numerous changes have been made to the application and database to improve reporting for partners.

The NMS application is helping to ensure that children are not being missed in the metabolic screening process in Alberta. While the application does not provide absolute certainty that all babies have been reached, the application is a useful tool to move towards that goal.